In the Specification:

Please replace the paragraphs starting on page 1, line 13 and ending on page 1, line 24 with the following paragraphs:

3. Field of the Invention

The present invention relates generally to mixing solutions and more specifically to a wrap spring clutch syringe ram which mixes precise amounts of solutions.

4. Discussion of Prior Art

There are two existing clutched rapid-reaction syringe rams. However, neither is commercially available. The first device is described by H. Gutfreund (Methods in Enzymology XVI, 1969, pp 229-249, ed. Kenneth Kustin, Academic Press, New York). Gutfreund used a 700 rpm motor coupled to a firmly engaging magnetic clutch and a magnetic brake. The microswitches which controlled the clutch and the brake were operated by a lever which moved with the syringe barrier.

Please replace the paragraph starting on page 2, line 20 and ending on page 3, line 9 with the following paragraph:

~~The~~ A non-clutched rapid-reaction syringe ram manufactured by Update Instruments (United States) is referred to in the Summary of Invention section. The Update Instruments design utilizes a low inertial DC motor coupled to an optical encoder. Manufacturers of non-clutched rapid-reaction syringe rams that utilize stepper motors include Bio-Logic (France), Hi-Tech (England), and KinTek (United States). The original rapid-reaction device of Hartridge and Roughton of 1923, placed each reactant into a separate, pressurized vessel, and drained the two solutions simultaneously from their respective vessels down

separate lines that joined together at a "Y". The reaction commenced at the "Y" junction, where the two solutions met and mixed, and the period of reaction was determined by the rate of flow of the mixed solution down the exit tube of the "Y", and by the volume of the exit tube, or delay line. The detector was placed at various points along the delay line, to monitor the extent of reaction verses period of flow after mixing.

Please replace the paragraphs starting on page 12, line 7 and ending on page 15, line 2 with the following paragraphs:

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a top view of a wrap spring clutch syringe ram in accordance with the present invention.

Figure 2 is a top view of the mixing section of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 3 is an end view of a clamping device for mounting syringes at a front of a syringe ram of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 4A is a schematic diagram of a computer, A/D converter, and linear potentiometer powered by a 24 volt supply in accordance with the present invention.

Figure 4B is a schematic diagram of a computer, A/D converter, and linear potentiometer powered by five ~~6 volt~~ 6-volt batteries in accordance with the present invention.

Figure 5 is a schematic diagram of a solenoid of a wrap spring clutch, trigger D/A output circuit, and computer in accordance with the present invention.

Figure 6 is a schematic diagram of a slotted photo interrupter, which serves to monitor the speed of the flywheel in accordance with the present invention.

Figures 7A is an end view of a rear moving block of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figures 7B is a top view of a rear moving block of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 7C is an end view of a front brass end piece which attaches with screws to a front of a threaded brass nut of a wrap spring clutch syringe ram and frit mixer in accordance with the present ~~invention. Figure 7D is~~ invention, together with a top view of a threaded brass nut of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure ~~7E~~ 7D is a ~~top~~ side view of a removable brass locking pin of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 7E is a bottom view of a removable brass locking pin of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 8A is a cross sectional view of a ~~plurality of typical~~ "cross" mixer ~~designs~~ design of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 8B is a cross sectional view of a "T" mixer design of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 8C is a cross sectional view of a "5-port" mixer design of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 8D is a cross sectional view of a “Y” mixer design of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 8E is a side view of an Upchurch ¼”-28 low pressure fitting of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 9A is a cross sectional view of a first frit mixer of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 9B is a cross sectional, frontal view of an Upchurch polymer-ringed frit of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 9C is a cross sectional, side view of an Upchurch polymer-ringed frit of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure ~~9B~~ 9D is a cross sectional view of a second frit mixer of a wrap spring clutch syringe ram and frit mixer in accordance with the present invention.

Figure 10 is a graph of an output of a linear potentiometer obtained during three pushes of a wrap spring clutch syringe ram in accordance with the present invention.

Figure 11 is a graph of an output of a linear potentiometer obtained during three pushes of a wrap spring clutch syringe ram in accordance with the present invention.

Figure 12 is a graph of dispersion of 0.025 sec pulses of dye (bromophenol blue + HCO_3^-) during flow through reaction delay lines of variable lengths of a wrap spring clutch syringe ram in accordance with the present invention.

Figure 13 is a graph of the responses of ~~an~~ a membrane inlet MAT 250 mass spectrometer to an injection pulse of water equilibrated with H_2 (mass 2), N_2 (mass 28), and C_2H_6 (mass 30) of a wrap spring clutch syringe ram in accordance with the present invention.

Figure 14 is a graph which compares progress curves for the reaction of $HCO_3^- + H^+ == CO_2 + H_2O$ of a wrap spring clutch syringe ram in accordance with the present invention.

Figure 15A is a side view of a <u>cam</u> wrap spring clutch syringe ram in accordance with the present invention.

Figure 15B is a top view of a rotating cam of a wrap spring clutch syringe ram in accordance with the present invention.

Figure 16A is a top view of at least one syringe actuated by the rotation of a cam of a wrap spring clutch syringe ram in accordance with the present invention.

Figure 16B shows a top view of a wrap spring clutch syringe ram with multiple cams with the lobes oriented radially in different directions and mounted on a single camshaft of a wrap spring clutch syringe ram in accordance with the present invention.

Please replace the paragraph starting on page 15, line 8 and ending on page 17, line 17 with the following paragraph:

Figure 1 presents a top view of a wrap spring clutch syringe ram. The syringes 10 are mounted at the front of the ram, and the flywheel 12 is mounted toward the rear of the ram. The flywheel 12 has substantial mass. The entire ram apparatus (except for the motor 14, DC motor speed control 16, computer 18, power supply 20, D/A converter 22, A/D converter 24, tachometer 26, and a few ancillary items, such as batteries, not shown in Figure 1, are preferably mounted on a 1/2 inch thick aluminum platform 28 of dimensions 46 1/2 inches long by 13 inches wide. In Figure 1, the top surface of this aluminum base 28 may be regarded as the plane of the sheet of paper. The ram itself is mounted firmly to the top of the aluminum platform 28 with twelve nylon screws (not shown) which pass upwards

from the underside of aluminum platform 28, through twelve small holes drilled through the aluminum sheet 28, and thence into holes drilled and tapped into the bottom of the four base supports 30A-30D. Nylon screws are used rather than metal screws, in hopes that the nylon screws will flex or break should any accidents occur with the ram. The position and alignment of these 12 holes in the aluminum sheet 28 is critical to the alignment and function of the ram, so these holes were drilled by first mounting the base aluminum sheet 28 on a Bridgeport milling machine. The total length of the ram, itself, from the back of support 30A to the front of support 30D is 30 3/4 inches. The distance from the back of support 30B to the front of support 30D is 24 inches. The distance from the back of the flywheel 12 to the front of the output hub 32 of the wrap spring clutch 34 is 5 1/2 inches. The front of output hub 32 is 1/4 inch from the back of support 30B. The distance from the front of support 30B to the back of support 30C is 6 3/4 inches. The centerline of the stainless steel shaft 36 and of the lead screw 38 is 3/4 inch above the top of the aluminum platform 28. The centerlines of the two parallel shafts 40 are also 3/4 inch above the top of the aluminum platform 28. The top of moving platform 42 is 2 inches above the top of stationary platform 28, and moving platform 42 is 18 inches long by 8 1/4 inches wide by 1/4 inch thick. The safety limit switch 44, and the linear potentiometer 130 are mounted with screws to the base aluminum sheet 28, also, and adjacent to moving platform 42 of the ram, as shown. A large hole 46 (~~dashed~~ thicker, dark line) is cut through the aluminum sheet to allow the 9 inch diameter flywheel 12 and the pulley 48A to extend through and below the aluminum sheet, and to rotate. A slot hole 50 (also ~~dashed~~ thicker, dark line) through the aluminum platform 28 extends outward from the hole 46 for the flywheel and pulley 48A to the outer periphery of the aluminum sheet 28, to enable the v-belt 52 to be

placed onto and around the pulley 48A and thereby to enable the v-belt 52 to extend from the hole 46, both above and below the aluminum platform 28 when joining the pulley 48A to the pulley ~~48A~~ 48B of the externally mounted motor 14. Once the v-belt 52 is in place, the slot 50 is covered with a removable 1/4 inch thick aluminum plate 54 which rigidly is screwed to top of the base aluminum sheet 28, to strengthen the area of the slot 50. The aluminum platform sheet 28 rests upon, and is bolted to wooden 4 X 4's (not shown), and the 4 X 4's rest upon and are bolted to an undergirding 3/4 inch thick sheet of exterior grade plywood (also not shown). The electric motor 14 is mounted rigidly to the top of the undergirding 3/4-inch-thick sheet of plywood, with the motor 14 to the side of, and with its centerline approximately 3/4 inch below the upper plane of, the aluminum sheet 28. Immediately prior to tightening the bolts which hold the motor 14 to the plywood sheet, the position of the motor 14 is adjusted with slots (not shown), so that the pulleys 48B and 48A are aligned, and the v-belt 52 is at the appropriate tension.

Please replace the paragraph starting on page 17, line 18 and ending on page 17, line 17 with the following paragraph:

The ram is composed of an electric motor 14 which drives a flywheel 12. Satisfactory operation has been found by employing either a 1/3 horsepower, 110 VAC, General Electric AC motor, model 5KC42JG25E, or a variable speed 1/4 horsepower General Electric DC motor, model 5BC 38PD1, controlled with a MagneTek W713 DC motor speed control 16. Input to the DC controller is 220 VAC, which yields twice the maximum horsepower of the DC motor compared with use of 110 VAC. Stepper motors, or motors of any type, also may be suitable. In our present system the output shaft of the motor

14 drives the flywheel 12 by pulley system 48A & , 48B, joined by a v-belt 52. Direct, or in-line, or geared, or chain, or notched belt, or variable speed gearbox, etc., drive systems may be preferred. The flywheel is preferably fabricated from 9 inch diameter x 1.75 inch thick piece of aluminum. The flywheel 12 is balanced, and rides upon a 1/4 inch diameter stainless steel shaft 36 via ball bearings 56A and 56B which are pressed fit into the center of the rear and front sides of the flywheel. Attached rigidly to the front side of the flywheel is the pulley 48A, and on the front side of the pulley 48A is mounted the rear input hub 62 of the wrap spring clutch 34. The pulley 48A and the rear input hub 62 of the wrap spring clutch 34 additionally are supported by an internal bearing (not visible) of the wrap spring clutch 34. The velocity of the flywheel is adjusted by the ratio of the pulleys 48A, 48B, or by adjusting the velocity of the DC motor 14 with speed control 16. The speed is monitored either by a calibrated stroboscope (not shown), or with a tachometer 26 coupled to a slotted photo interrupter 58. The flywheel is fitted on its front side with a protruding ring 60 fitted with a series of twenty-five evenly spaced slots. The slotted ring 60 fits into the slot of the slotted photo interrupter 58, between the light source and photo detector of the photo interrupter 58.

Please replace the paragraph starting on page 18, line 23 and ending on page 20, line 9 with the following paragraph:

On the front side of the flywheel is attached the pulley 48A, and the pulley 48A is mounted rigidly to the rear input hub 62 of the wrap spring clutch 34. Note that the flywheel 12, pulley 48A, and the rear input hub 62 of the wrap-spring clutch 34 are bolted together (with three long machine screws - not shown) to form a single unit, through which

the 1/4 inch diameter stainless steel shaft 36 passes. The flywheel 12, pulley 48A, and the rear input hub 62 of the wrap spring clutch 34 spin together as a single unit, on ball bearings 56A and 56B, and on the internal bearing (not visible) of the wrap spring clutch 34. Shaft 36, lead screw 38, plus front output hub 32 and stop collar 64 of the wrap spring clutch 34, usually are stationary, however whenever the wrap spring clutch 34 is engaged, stop collar 64, the front output hub 32, shaft 36, and lead screw 38 rotate together with the flywheel 12, pulley 48A, and rear input hub 62. Model CB-2 wrap spring clutch 34 is manufactured by Warner Electric. There are many models, sizes, and manufacturers of wrap spring clutches; units of other sizes from Warner Electric, or wrap spring clutches from other manufacturers also may be suitable. The wrap spring clutch 34 employs a 2-stop collar 64. This collar 64 preferably has two equally spaced stop notches per one rotation, meaning that the clutch may be engaged for a minimum of 1/2 rotation. Several other stop collars are available from Warner Electric, ranging from 1-stop to 24 equally spaced ~~stops;~~ stops and may be substituted. ~~clutches~~ Clutches fitted with these collars can be engaged for a minimum of 1 rotation, or 1/24th rotation, respectively. Or stop collars, perhaps with unequally spaced stops, or a nonstandard number of stops, etc., may be custom made. The front output hub 32 of the wrap spring clutch 34 is attached rigidly to the central 1/4 inch diameter stainless steel shaft 36, by one Allen screw 66, so that when output hub 32 rotates, shaft 36 rotates. When shaft 36 rotates, shaft 36 turns lead screw 38. The front mounting plate 68 of the wrap spring clutch is restrained from rotating by a pin 70. Pin 70 is rigidly mounted with screw threads into the rear of stationary mount 30B. Pin 70 is inserted through a hole in the mounting plate 68, such that movement of the mounting plate 68 is not restrained axially. This method of mounting is recommended by Warner Electric because it prevents rotation

of the mounting plate 68 while reducing the load on the internal plate bearing (not visible) of the clutch 34 ~~(see enclosed page E-47 of Warner Electric catalog, Figure 1)~~.

Please replace the paragraph starting on page 20, line 10 and ending on page 22, line 8 with the following paragraph:

Starting from the rear of the ram assembly, the 1/4 inch diameter stainless steel shaft 36 passes through ball bearing 72A, which is pressed fit into end support 30A. Shaft 36 then passes through ball bearing 56A at the rear of the flywheel 12, and through ball bearing 56B at the front of the flywheel 12. Shaft 36 continues through the flywheel 12, pulley 48A, and the rear input hub 62 of the wrap spring clutch 34, all three of which are rigidly bolted together to form a single assembly, as previously mentioned. After passing through the wrap-spring clutch assembly, shaft 36 then passes through ball bearing 72B which is pressed fit into a hole which is machined part-way into the back side of, but not through, support 30B. Shaft 36 then passes through a smaller diameter hole (circa 1/4 inch diameter) drilled the remainder of the way through support 30B, and thence through thrust bearing 80A on the front face of support 30B. The front end of shaft 36 extends into and terminates in a hole 82 drilled into the rear of the lead screw 38. In our design, the 1/4 inch diameter stainless steel shaft 36 is a separate piece from the lead screw 38. A 1/4 inch diameter hole 82 is drilled into the center, rear, of lead screw 38. Shaft 36 is held firmly within hole 82 of lead screw 38 by an Allen screw 84, such that shaft 36 and lead screw 38 rotate together as a single unit. Lead screw 38 is an acme screw of 316 stainless steel, machined by us on a Hartridge Lathe. The outside diameter of lead screw 38 is 1/2 inch, and its pitch is 4 turns per centimeter. A more expensive, precision stainless steel ball screw fitted with a

preloaded ball nut probably would be superior to our stainless steel acme screw in this application. Lead screw 38 passes through brass nut 90 which is of internal diameter 1/2 inch, and is threaded on ~~the~~ its inside diameter at pitch 4 turns per centimeter. Brass nut 90 is 0.915 inch in outer diameter, is round on its outer circumference, and is machined to fit closely within a hole of 0.915 inch internal diameter drilled axially from the rear to the front through aluminum moving block 92. The lead screw next passes through brass front end piece 93 which is held to the front face of Brass nut 90 with screws. The brass nut 90 is prevented from rotating and is held firmly within aluminum moving block 92 by a removable, round, brass pin 94 which fits snugly into a 3/4 inch diameter hole drilled into the top of moving block 92. A smaller diameter extension on the bottom center of pin 94 extends snugly into a 1/4 inch diameter hole drilled into the top of brass nut 90. Thus removable pin 94 firmly holds nut 90 within moving block 92, and prevents nut 90 from rotating when acme screw 38 rotates. Removable pin 94, brass nut 90, front end piece 93, and block 92 will be described in more detail in ~~Figure 7~~ Figures 7A-7E.

Please replace the paragraph starting on page 22, line 9 and ending on page 23, line 1 with the following paragraph:

The remainder of the apparatus includes a precision slide with precision syringes and a rapid-mixing device mounted in front of the slide. Passing through supports 30B, 30C, and 30D are two, parallel, two-feet-long, 3/8-inch diameter, precision-ground, hardened steel shafts 40. These shafts are 7 3/8 inches apart, center to center. These two hardened shafts 40 additionally pass through linear ball bearings 96 which are pressed fit into holes drilled through moving block 92 and push block 95, near the outer edges of blocks 92 and

95 in the positions shown. Sleeve bushings also can be substituted for the linear ball bearings 96. Rigidly mounted with screws atop moving block 92 and push block 95, and joining the two blocks rigidly together is a 1/4-inch-thick aluminum sheet of dimensions 8 1/8 inches wide, by 18 inches long, which forms a moving platform 42. Platform 42, designated in Figure 1 by a thicker peripheral line, is attached to, joins, and covers both moving blocks 92 and 95. Platform 42 joins, spans, and covers points A, B, C, and D. Platform 42 does not make contact with support 30C, or with shafts 40. The platform 42 glides on the linear roller bearings 96 within moving block 92 and push block 95 as they glide along the shafts 40, as moving block 92 is driven by rotation of the lead screw 38 within nut 90. The platform 42 is longer than it is wide to ~~significantly~~ reduce significantly side-to-side wobble of the platform 42 as it moves along the shafts 40.

Please replace the paragraph starting on page 23, line 2 and ending on page 23, line 11 with the following paragraph:

At the front of the platform 42 and on the front face of the push block 95 is mounted a flat, 1/8 inch thick aluminum plate 98. The plate 98 is positioned to push the plungers 100 of the syringes 10. Any number of syringes 10 may be used, and these syringes 10 are mounted securely onto or in front of support 30D. With reference to figure 2, it is preferable to use 1 ml, or 0.5 ml "C"-type Hamilton gas-tight syringes 10 in our application.
The "C"-type syringe is equipped with a male, threaded 1/4"-28 fitting 126, which enables leak-tight coupling of this syringe to lines, mixers, etc. In Figure 2 a ¼"-28 male fitting 126 of a “C”-type Hamilton syringe is joined to a section of 1/16” O.D. stainless steel tubing 130

by means of an internally threaded union 128, a ferrule 252, and a ¼"-28 Upchurch male fitting 250.

Please replace the paragraph starting on page 23, line 11 and ending on page 24, line 5 with the following paragraph:

With reference to figure 3, the syringe mounts are constructed by drilling holes 102 of slightly smaller diameter than the syringe barrels 10 through a flat sheet of plastic. The plastic sheet then is cut in half, such that the holes 102 are cut in half longitudinally. One half 103 of the plastic piece is laid below the syringe barrel(s) 10, and the second half 104 is placed above the syringe barrel(s) 10 with each syringe barrel resting in the hole that was drilled for it. ~~With reference to figure 3, machine~~ Machine screws 105 then are passed through additional holes 106 drilled vertically through the plastic mounting pieces (only five of the eight vertical holes 106 are labeled in Figure 3). The holes 106 are of slightly larger internal diameter(s) than the external diameter(s) of the threaded portion(s) of the machine screws 105. These screws 105 extend into tapped holes 107 drilled into the top of end support 30D. The upper 104 and lower 103 plastic pieces then are tightened firmly together and firmly to the top of support 30D by tightening the machine screws 105 into the threaded holes 107, thus clamping the syringe barrel(s) 10 securely in place. The ends of the 3/8 inch diameter shafts 40, that pass into piece 30D are displayed in Figure 3, as well.

Please replace the paragraph starting on page 24, line 6 and ending on page 25, line 1 with the following paragraph:

<u>With reference to Figures 1 and 2, the</u> ~~The~~ outlet of each syringe 10 is connected to a three-way valve 108. Three types of small volume, three-way valves have been employed. All three types work suitably at the pressures generated within the system. One is a three-way valve with a tapered, Delrin, rotating central stem. A six-port, Rheodyne HPLC valve is modified to enable its use as a dual three-way valve. A modified 4-port, Upchurch V-100T, injection-molded, 3-way switching valve may also be used. When rotated to the appropriate position, each three-way valve 108 enables filling of its attached syringe with the designated reactant solution 110, 112 contained in its reservoir 114. Prior to activating the ram, both three-way valves 108 are manually rotated appropriately, to isolate their respective reservoirs 114, and to enable the contents of each syringe 10 to empty through its line 116 to the mixer 120 when the plungers 100 simultaneously are pushed by the ram. After exiting the mixer, the mixed solutions travel through reactor line 122. Figure 2 shows the frit mixer 120, and additionally a detector 124 placed along reactor line 122. The detector 124 often is a spectrophotometer, or may be a mass spectrometer equipped with a flow-through membrane inlet, etc. Alternatively, the solution exiting the reactor line may be quenched chemically, or by freezing, etc., and saved analysis.

Please replace the paragraph starting on page 25, line 2 and ending on page 25, line 15 with the following paragraph:

<u>With reference to Figure 1, the</u> ~~The~~ motion and position of the moving platform 42 are monitored with a linear potentiometer 130. The linear potentiometer 130 is mounted such that its tang 132 can be pushed by front piece 98 (which is mounted to the front of push block 95) as the platform 42 moves forward. The linear potentiometer 130 is mounted on a

base containing slots (not shown), so that the body of the linear potentiometer 130 can be repositioned axially along the side of the platform 42, and remounted securely to the aluminum base 28 by retightening the same screws. The analog output from the linear potentiometer 130 is fed into an A/D converter 24 and thence into a computer 18 for storage and later analysis. The electrical connections to and from the linear potentiometer 130 will be described below, with reference to Figure 4, together with the analog to digital input A/D converter board 24.

Please replace the paragraphs starting on page 27, line 2 and ending on page 28, line 2 with the following paragraphs:

Figures 4A-4B and 5 show diagrams of the electronics which control and enable monitoring of the wrap spring clutch syringe ram. Electrical connections to the solenoid 134 of the wrap spring clutch include the power supply 20, the solid state relay 140, the manual on-off switch 138, the safety limit switch 44, the digital to analog output (D/A) board 22, and the computer 18. The aluminum plate 98 attached to the front of block 95 of the ram platform 42, pushes not only the syringe plungers 100, but also the sliding tang 132 of the linear resistor 130.

The circuitry connecting to and from the linear potentiometer 130 is depicted in ~~Figure 4~~ Figures 4A and 4B. The linear potentiometer 130 when coupled with the time base of the computer enables us to monitor the position of the ram with respect to time. The linear potentiometer 130 presently used on the machine is a 10 K ohm, Model 422 DD, Slideline potentiometer manufactured by Duncan Electronics, Inc., Costa Mesa, California, USA. It may be powered from a home-built power supply 150 (Figure 4A), which delivers

+24 and -24 volts DC relative to a commonly grounded terminal. Connecting the linear potentiometer 130 to the power supply, with inclusion of an additional 6800 ohm resistor 152 between the -24 Volt terminal of the power supply, and terminal 1 of the linear potentiometer, as shown, enables adequate motion-to-voltage response, together with use of the full 4096, 12 bit (2^{12}) range of the analog to digital (A/D) converter 24 which is installed in a 386/40 MHz computer 18. A plug-in, Labtech PCL 711 A/D - D/A board with 8 input channels is used, and each input channel responds to analog input voltages between -5 and +5 volts.

Please replace the paragraph starting on page 28, line 9 and ending on page 29, line 3 with the following paragraph:

With reference to Figure 5, the ~~The~~ computer sends a 5 volt pulse, on que, from the Labtech PCL 7ll digital to analog (D/A) converter board 22 to the control terminals of the solid state relay 140. A Crydom relay is used with ODC, 5A AC output, DC output 1A at 200VDC, DC control 2.5 - 8 VDC, #429105. Across the control leads of the relay 140, a 560 ohm resistor 158 has been included and an LED 160, which blinks when the computer sends an output pulse. The negative output terminal of the relay 140 is connected to one terminal of a manual on-off switch 138, which also can serve as a manual safety shut-off switch. To the second terminal of this on-off switch 138 is connected an adjustable position safety limit switch 44. This safety limit switch 44 is affixed to a base containing mounting slots (not shown), such that this switch 44 may be moved axially adjacent to the platform of the ram, and positioned such that when and if the front of the ram platform 42 moves too far forward, such that further forward motion of the ram risks the breaking of syringes, etc., the

safety limit switch will be tripped open by the front plate 98 of the ram. Once the safety limit switch is tripped open, power to the ram solenoid immediately is switched off, thus disengaging the wrap spring clutch, and quickly halting further forward motion of the ram.

Please replace the paragraph starting on page 30, line 16 and ending on page 30, line 21 with the following paragraph:

The circuit diagram of the slotted photo interrupter 58 is shown in figure 6. A separate 5 volt DC power supply is employed. Light emitted from the light emitting diode (LED) 141 is collected by the phototransistor 142. With photointerrupter 58 properly mounted in position next to the flywheel 12, the slotted ring 60 which protrudes from the flywheel 12 is located between the LED 141 and the phototransistor 142. As the flywheel 12 rotates, the slots of the slotted ring 60 interrupt momentarily and repeatedly transmission of light from the LED 141 to the phototransistor 142. The resulting electrical pulses pass through the circuit of Figure 6, which includes a 2200 ohm resistor 146, and a 200 ohm resistor 144, to produce an output signal 148. The detected output signal 148 can be stored by the computer 18, via an input channel of the A/D converter 24, or fed into a counter-timer, frequency counter, or tachometer 26 to clock the rotational velocity and performance of the flywheel 12.

Please replace the paragraph starting on page 30, line 22 and ending on page 31, line 3 with the following paragraph:

A calibrated strobe light (Strobotac type 631-BL, General Radio Company, Cambridge, Massachusetts) is used to monitor the velocity and relative position of the

flywheel 12. Another accurate method to determine the velocity and position of a spinning flywheel is to place a known number of equally spaced dots around the periphery of ~~his~~ the flywheel, and to use ~~used~~ the known cycle rate of fluorescent lighting of 7200 cycles per minute to clock the speed.

Please replace the paragraph starting on page 31, line 4 and ending on page 31, line 10 with the following paragraph:

A Tektronix Inc. Type RM564 storage oscilloscope equipped with a plug-in Type 3A9 differential amplifier and a plug-in Type 2B67 timebase ~~is~~ can be used to record the output traces of the linear potentiometer 130. ~~The~~ Any suitable recording oscilloscope can be used successfully in place of the A/D converter and the 386 / 40 Megahertz computer to record and to measure these and other fast responses.

Please replace the paragraph starting on page 32, line 15 and ending on page 32, line 23 with the following paragraph:

The results of the push may be viewed on the computer screen corresponding to the readings of 8 input channels. The 12 bit A/D converter presents numbers which range from 0 to 4095, corresponding to -5 to +5 volts. It is possible to adjust the various inputs, and/or the ram position/linear potentiometer, and/or any amplifier gains or zero offsets, etc., to insure that the input readings are on scale. The data from an executed run is stored automatically as 8 ASCII files, one for each input channel.

Please replace the paragraphs starting on page 34, line 13 and ending on page 37, line 19 with the following paragraphs:

Figures ~~7A & 7B~~ 7A-7E show views of the rear moving block 92, the brass front end piece 93, the threaded brass nut 90, and the brass locking pin 94 ~~94, and the brass front end piece 93~~. The purpose of the rear moving block assembly is to enable the sliding platform 42 to move forward, coupled precisely with the starting, stopping, and rotation of the lead screw when the locking pin is in place, and to enable reversal of the sliding platform 42 to its original position by manual rotation of the threaded brass nut 90 after one or multiple pushes of the ram, when the locking pin 94 is removed. The moving block 92 (Figure 7A) is preferably fabricated from solid aluminum and has four precisely reamed through-holes. Its dimensions preferably are 8 ¼ inches wide x 1 ½ inches high x 1 ¼ inches deep. Centrally located at the top is a raised section 169 measuring ¼ inch high x 13/16 inch wide. The two axial holes 166 are spaced 7 ¾ inches apart, center-to-center, and ~~The two axial holes 166~~ each axial hole 166 accommodates a pressed fit sleeve roller bearing 96 through which the two 3/8 inch diameter hardened steel rails 40 of the slider pass. Sleeve bushings can be substituted for the sleeve roller bearings 96. An axial central hole 168 of 0.915 inch diameter accommodates with close tolerances the threaded brass nut 90, which rides along the acme lead screw 38. The top view of the moving block 92 (Figure 7B) displays a central vertical hole 170 of ¾ inch diameter into which the removable brass locking pin 94 inserts with close tolerances.

The cylindrical threaded brass nut 90 (Figure 7C) rides smoothly, without wobble along the stainless steel lead screw 38, and fits into the rear of hole 168 of the aluminum moving block 92. The brass nut's narrower portion of 0.915 inch diameter, passes

completely through hole 168 of the moving block 92 with close tolerances. The front face 171 of the larger, 1.5 inch diameter rim of the threaded brass nut 90 contacts the rear of the moving block 92, and prevents the nut 90 from passing all the way through the block 92. The preferred measurement of nut 90 from front face 171 to the front edge 175 is 1 ¼ inches. When the nut 90 is properly in place, its front edge 175 extends slightly beyond the front face of the moving block 92, such that the brass front end piece 93 may be attached tightly to the front face of the nut 90 with two screws. The hole through the center of end piece 93 is of 9/16 inch internal diameter so that the 1/2 inch diameter lead screw 38 easily is able to pass through it. When the nut 90 is in the moving block and the front end piece 93 is rigidly attached with screws to the nut 90, the nut 90 is freely able to rotate along the acme lead screw 38, and within the moving block 92, even though all tolerances of the nut 90 and front end piece 93 in front of, behind, and within the moving block are close. The outer, 1/4-inch-wide, outside edge 173 of the larger, 1/4 inch x 1.5 inch rear portion of the nut 90 is knurled (by example, and not by limitation), so that the nut 90 may be grasped with the fingers, and rotated easily while nut 90 is mounted within the moving block 92. When nut 90 is mounted properly in the moving block 92, and when the front end piece 93 is properly attached with screws to the front of nut ~~90. The~~ 90, and when the entire system is assembled as in Figure 1 except that the locking pin 94 is ~~removed. The~~ removed, and when the lead screw is prevented from rotating by the internal springs of the wrap spring clutch 34 due to the wrap spring clutch being ~~disengaged. Next,~~ disengaged, then manual rotation of the nut 90 causes the moving block, and the entire platform 42 to glide forward along the rails 40 when the nut 90 is screwed clockwise, or backwards along the rails 40 when the nut 90 is screwed counterclockwise (as viewed from the rear of the ram). The lead screw and nut in

the constructed example are of right-handed thread, though left-handed thread could be used were the direction of the wrap spring clutch reversed from our present model. The outer diameter of front end piece 93 is 1 1/8 inch, which is larger than the 0.915 inch diameter central axial hole 168 through the moving block. Thus the primary purpose of end piece 93 is to pull the moving block 92 backwards along with nut 90, when nut 90 manually is rotated counterclockwise. Front end piece 93 also may assist locking pin 94 in preventing further forward motion of the moving block 92 when rotation of the lead screw is stopped by the wrap spring clutch at the end of a push.

The removable brass locking pin 94 (Figures 7D and 7E) fits with close tolerances fully down into hole 170 in the top of the moving block 92, until the lower face 177 of the 1 1/4 inch diameter rim 179 of ~~the~~ locking pin 94 touches the top of ~~the~~ moving block 92. Though a snug fit, locking pin 94 easily can be inserted into or removed from its hole 170 in moving block 92, with the fingers. Both the cylindrical body 95 of locking pin 94, and the hole 170 into which locking pin 95 inserts, are ¾ inch in diameter. Machined in the center of the locking pin 94 at its bottom is a 0.2 inch long by 1/4 inch ~~wide~~ diameter round extension pin 172 that fits with close tolerances into a corresponding hole 174 also of ¼ inch diameter drilled into the top center of threaded brass nut 90. To engage extension pin 172 with hole 174 of the brass nut 90, the removable locking pin 94 is inserted into hole 170 of the moving block 92, ~~and~~ with the fingers simultaneously rotating the threaded brass nut 90 slowly within the moving block until the hole 174 and the pin 172 line up. Locking pin 94 then can be pressed fully into the moving block 92, and into hole 174 in nut 90; nut 90 will be locked into place, unable to move forward or backwards even slightly, or to rotate, within the moving block 92. Because the wrap spring clutch is unirotational, movement of the

platform assembly 42 may only occur in a forward direction only if and when the lead screw 38 is turned counterclockwise by engagement of the wrap spring clutch with the rotating flywheel. A system employing a left-hand threaded lead screw and nut, with a clockwise wrap spring clutch would work equally as well.

Please replace the paragraphs starting on page 38, line 1 and ending on page 39, line 13 with the following paragraphs:

If the lead screw drive was omitted, and replaced with a revolving, snail-shell-like, sloping cam 260, as in Figures 15A-B and 16A-B ~~Figure 15~~, a mechanism for reversal of the cam would not be necessary. Instead the cam could be advanced by engagement of the wrap spring clutch until the cam lobe had rotated past its peak, or to an appropriate minimum, thereby enabling refilling of the syringes, and initiation of a new run. Additionally, were a manually removable locking pin 270 inserted through the cam, removal of the locking pin would enable uncoupling of the rotating cam from the unidirectional wrap spring clutch, to enable manual repositioning of the cam.

A plurality of mixing devices are shown in ~~figure 8~~ Figures 8A-8D. These mixers employ standard 14"-28 flat-bottomed, 3/8 inch deep, female fittings, which ~~allows~~ allow leak-tight connections to be made with commercially available 1/4"-28 low pressure male fittings 250, available from Upchurch Scientific (Figure 8E). The Upchurch male low-pressure fitting 250 consists of a plastic piece with a knurled portion 253 and a threaded portion 255. The knurled portion is 3/8 inch diameter x 3/8 inch long. The threaded portion uses ¼"-28 threads and is ½ inch long. Through the center of the plastic piece is a hole through which the 1/16 inch tubing 254 passes. The through hole is flared at one end to

accommodate the ferrule. The tubing 254 passes with close tolerances through a hole in the center of the ferrule 252. A 1/4"-28 male plastic fitting has been employed which is manufactured by Valco Instruments, and which ~~are~~ is similar to those fittings manufactured by Upchurch, except that ~~they employ~~ it employs an additional collar bushing between the threaded piece and the ferrule. The internal tube diameters within the plurality of mixers of Figures 8A-8D range from 0.010 inch to 0.0135 inch. The external diameters of these mixers preferably are 1 inch. The mixer design types displayed are "Cross" 180, "T" 182, "Y" 186, and "5-port" 184 ~~mixer designs~~.

Valco makes some "micro volume connectors" shaped as "T"'s, "Y"'s and "Crosses". These narrow-bore connectors use high-pressure ferrules and nuts manufactured by Valco that are not of the 1/4"-28 design. These connectors are composed of various materials, including stainless steel, and have a removable outer ring and a central insert. The removable outer ring contains the female threads which hold the male nut connector. Machined into the central insert are the narrow-bore through holes, and the seals for the ferrules. This ring/insert design enables the machinists at Valco to drill the insert with short holes as narrow as about 0.006 inch I.D.

Additionally the "grid mixer" has been employed which is manufactured by Update Instruments (not shown). The grid mixer is essentially a "T" mixer, which uses a series of closely spaced, very fine mesh screens immediately downstream from the point of mixing, to generate turbulence. The introductory jets of the Update grid mixer are 0.008 inch I.D.

Please replace the paragraph starting on page 41, line 18 and ending on page 42, line 5 with the following paragraph:

Next, the male portion 202 of the mixer is screwed into the body of the female portion 200, such that the outlet cone 228 of male portion 202 is centered just below, and firmly against, the bottom outlet of the frit 222. With the male portion 202 in this position, the flat portion of the upper surface 230 of the ~~female~~ male portion 202 presses tightly against the bottom of the teflon sleeve, thus making a water-tight seal around the frit, and between the male and female portions. Now solutions that enter through the inlet ports 210 and 212 of the female portion 200, will meet at the "T" junction 214, flow through the short tube 216, then through the cone 220, thence into and through the frit 222, out through cone 228, and to the outlet of the mixer. When female and male portions are fully assembled together, this frit mixer is preferably 1 inch in diameter by 7/8 inch high.

Please replace the paragraph starting on page 44, line 6 and ending on page 44, line 21 with the following paragraph:

When designing mixers, others logically have attempted to introduce barriers to flow that would generate and/or initiate turbulence. The grid mixer of Update instruments is one example. Grids are known to generate turbulence, and therefore mixing, and this turbulence can be described theoretically. Another mixer that can be described theoretically, the Berger Ball mixer, introduces a spherical ball into the flowing stream, to generate turbulence downstream from the ball. A random pile of debris in the form of a porous stainless steel frit was placed in the path of the mixing solutions. It seemed that the random maze of narrow rivulets generated within the frit probably would initiate turbulence, as the

randomly-placed rocks in a river generate rapids, and would complete the job of mixing the solutions that first began when the solutions first collided at the mixing "T" junction 214, even if it might be impossible to describe the random mixing within the frit ~~mathematically, such~~ mathematically. Such appears to be the case.

Please replace the paragraph starting on page 44, line 22 and ending on page 46, line 4 with the following paragraph:

Another, simpler route to constructing a frit mixer is to machine, or to purchase from Valco Instruments, a "T", "Y", "Cross", etc., and to obtain a frit from Upchurch Scientific. With reference to ~~figure~~ Figures 9B-9C, Upchurch markets frits of many different materials, including PEEK, ultra-high molecular weight polyethylene, titanium, and stainless steel. The advantage of the Upchurch frits ~~238~~ 242 is that they may be obtained surrounded on their periphery with a polymer ring 240, to produce the Upchurch polymer-ringed frit 238. The frit 242, itself, is of dimensions 1/16 inch diameter, by 1/16 inch thick. The polymer rings 240 are 1/4 inch diameter by 1/16 inch thick, and the frit 242 is held firmly in a 1/16 inch diameter through-hole in the center of the polymer ring 240. This polymer ring 240 serves the same purpose of making a seal around the sides of the frit, as does the teflon tube/sleeve 224 that surrounds the frit 222. By inquiry from Upchurch, one can obtain frits with larger pore sizes, above 20 microns. Then, with reference to Figure 9D, one drills a small cone 244 of maximal diameter 1/16 inch in the bottom well of the 1/4"-28 female outlet hole 246 of a "T", "Y", or "Cross", etc., mixer 248 (~~Figure 8,~~ Figures 8A-8D, Figure ~~9B~~ 9D). Next, one simply inserts one of these Upchurch frits + polymer rings 238 into the slightly modified 1/4"-28 female exit hole 246 of the mixer 248. The frit + polymer ring

238 is held in position in the female 1/4"-28 well 246, by screwing a male, low-pressure Upchurch fitting 250 and ferrule 252 into the outlet hole 246. This male outlet fitting 250 and ferrule 252 also hold the reactor line 254. One pulls the 1/16th inch O.D. outlet reactor tube 254 back slightly in its ferrule 252, to make a "cone-like" exit space 256 immediately on the down-stream side of the frit 238, or alternatively carefully drills a small cone 256 into the tip ~~256~~ of the 1/16 inch O.D., outlet reactor line 254, to enable solvent to exit the frit 238 and to pass more readily into the narrow-bore of the reactor tube 254. These simple-to-construct frit mixers work well, and probably mix significantly more quickly and efficiently than do the simpler "T", "Y", "Cross", etc., mixers which lack the frit, and which rely solely upon their narrow-bore jets to generate turbulence, and to effect mixing.

Please replace the paragraph starting on page 47, line 12 and ending on page 48, line 7 with the following paragraph:

Figure 10 shows a graph of output traces of the linear potentiometer 130 from the second of the 5 pushes of the ram, from 3 of the 4 runs of the program. A computer-triggered, 4 msec pulse is also shown from the power supply 20 to the solenoid 134. The graph in figure 10 shows just how reproducible each push of the ram is. Please note that the clutch 34 engages fully 12 msec after initiation of the 4 msec computer pulse. Starting and stopping of the ram is very rapid, and may be nearly instantaneous on this time scale. Further, the rate of motion is constant and uniform during each push. The duration of each of the three pushes is measured in ~~figure~~ <u>Figure</u> 10 with a ruler and <u>is</u> estimated to be 25.3 msec. The predicted time for 1/2 rotation of our flywheel at 1200 rpm is 25 msec (the two-stop wrap spring clutch engages for 1/2 turn). Note that interestingly, the output of the

linear potentiometer 130 from each of these three pushes is exactly superimposible; even the noise during three separate pushes is invariable. Thus, each of the three runs is identical within the ability to measure it, with every push yielding the same, single line. In these experiments, ~~pushing~~ pushes were performed reproducibly along the same sections of the ram, and simultaneously along the same segments of the linear potentiometer 130. The results are always identical for each push along the same ram/linear potentiometer segments.

Please replace the paragraphs starting on page 57, line 25 and ending on page 58, line 23 with the following paragraphs:

When a wrap spring clutch is fitted with a multiple-stop collar, the ~~ram~~ wrap spring clutch can rotate the cam, and push the syringe plungers, incrementally, in as many increments of a full circle or of a full displacement, as there are stops on the stop collar. For example, when fitted with a one-stop collar, a ~~wrap-spring~~ wrap spring clutch would rotate the cam a minimum of one full revolution per engagement, and a 4-stop collar would rotate the cam a minimum of 90 degrees, each time a momentary electrical pulse were delivered to the solenoid. With the 1-stop collar, the syringe would be displaced to the full extent of the cam on one engagement of the clutch. With a 4-stop collar, the syringes could be displaced at minimum 1/4 the displacement of the cam, per engagement of the wrap spring clutch. The velocity of each push could be varied by varying the velocity of the flywheel by varying the speed of the electric motor, or by varying the ratio of the pulleys between the electric motor and the flywheel.

With reference to figure 16A, a rotating camshaft containing multiple cams could be employed with the relative angle of the lobe of each cam being adjustable relative to the

other cams. Further, were each cam to push a separate cam follower, this arrangement would yield the possibility of pushing any of several syringes, each syringe mounted on the front of a separate slide, so that each syringe could be pushed at a specified time. ~~The~~ Thus a slide ~~in figure 16~~ of Figure 15A could be omitted, and a syringe plunger could be pushed directly by the cam follower 272, itself, as in Figure 16A.

Please replace the paragraph starting on page 59, line 10 and ending on page 60, line 3 with the following paragraph:

The disadvantages of the cam design are two. First, if the cam rotates beyond its lobe 265 to a minimum 282, there no longer is any mechanical restraint behind the cam follower and the push platform to prevent a high back pressure in the syringes from reversing the ram. Second, when there is little back pressure or friction in the syringes, there is little to prevent the slide from continuing to advance on its own momentum, after the wrap spring clutch first has accelerated the platform to speed, and then has stopped rotation of the cam. Thus, though the braking action of the wrap spring clutch will stop the rotation of the cam quickly, the cam follower 272 and pushing platform 42 might continue to advance forward on their own momentum after the cam has stopped pushing. These two disadvantages of the cam design are not problems for the lead screw design (Figure 1), in which the push platform 42, nut 90, lead screw 38, and wrap spring clutch 34 are tightly coupled, both fore and aft. With the lead screw design, the nearly instantaneous accelerating and braking properties of the wrap spring clutch, and also the wrap spring clutch's ability to hold firmly against a load in both the forward and reverse directions are utilized where needed, on the syringe ram platform 42, itself.

Please replace the paragraph starting on page 60, line 4 and ending on page 60, line 17 with the following paragraph:

It is assumed even with the screw-driven system that back pressure in the syringes, or the friction of the plungers 100 in the syringe barrels 10, is sufficient to prevent further advance of the plungers 100 on their own momentum after the ram has stopped. However, the rear tips of the syringe plungers 100 ~~are~~ can be ~~threaded, and are~~ threaded and screwed into ~~the~~ threaded ~~ends~~ holes in the push plate 98, to make a tightly coupled system. The only apparent drawback of the lead screw design compared with the cam design is that with the lead screw design some means must be available to enable decoupling of the push platform from the irreversible, unidirectional wrap spring clutch, to enable retraction of the push platform, and refilling of the syringes. The removable locking pin/manually reversible nut assembly is both simple and effective, and is one of several possible solutions to this difficulty.

Please replace the paragraph starting on page 60, line 18 and ending on page 61, line 12 with the following paragraph:

Rapid-reaction rams can be used for at least three types of kinetic techniques. These include stopped-flow, continuous-flow, and push-pause-push. Stopped-flow studies require a ram that can push two reactant solutions together rapidly, and then stop their flow instantly. Usually, stopped-flow uses pressurized gas and a piston to push syringes, and a stop syringe to stop the flow. Observation of the mixed solutions occurs through an observation cell located immediately downstream from the point of mixing, and observation

is begun at the moment when flow stops. The wrap spring clutch syringe ram, because it can accelerate and decelerate so quickly, should be very effective for the stopped-flow technique. Because stopped-flow ~~apparatus~~ apparatuses presently use both gas-driven pistons, and stop syringes, the pressures generated in the reaction solution can be quite high, and pressures may generate artifacts and/or affect reactions. For example, pressure-generated spikes have been generated when working with pH indicators with gas-driven stopped-flow machines. Use of a wrap spring clutch syringe ram should avoid these pressure anomalies, especially since no stop syringe is necessary. On the other hand, the wrap spring clutch syringe ram can start and stop the flow of solutions so quickly that effects due to water hammer may arise.

Please replace the paragraph starting on page 62, line 8 and ending on page 63, line 3 with the following paragraph:

The push-pause-push method is a variant of the continuous flow technique. In this method a single reactor line of constant length is used. The syringes are pushed at a constant velocity by the ram, and the mixed reactants are flowed rapidly into the delay line. However, before the reactants reach the detector, flow is instantly paused. The reactants then are allowed to incubate, or to age, in the reactor line during the pause, as the solution remains stationary in the line. After a predetermined pause time, flow immediately is ~~immediately~~ reinitiated, and the reactants then are expelled from the reactor line for collection, or into or through a detector, by this second push, usually by the same ram. Although the pumping speeds of the two pushes can be varied, the pumping speed usually is held constant and normally is of the same velocity during both pushes. Different reaction

times normally are obtained by varying the duration of the pause. The age of the solution is the sum of the two flow times necessary for the solution to traverse from the mixer to the detector, plus the pause time. Because the wrap spring clutch syringe ram is able to start and to stop almost instantly, and to flow at a defined rate during the push, and because successive pushes are easily performed after a programmable pause of any desired length, the wrap spring clutch is well suited for performing the push-pause-push technique.